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| 09/857,518 | 12/12/2001 | Asaph Aharoni | 4916US | 5379 |

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EXAMINER

SAIDHA, TEKCHAND

| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/857,518

Applicant(s)

AHARONI ET AL.

Examiner

Tekchand Saidha

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-21, 34, 43, 45 and 46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 45 is/are allowed.
- 6) ☒ Claim(s) 19-21, 34, 43 and 46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Final rejection

1. Applicants Amendment filed 15 November, 2004, is acknowledged.
2. Claims 19-21, 34, 43 (amended) and 45-46 (new) corresponding to SEQ ID Nos. 6 and 31, are pending and under consideration in this examination.

3. **Claims withdrawn** :

Claims 1-18, 22-33, 35-40 (fully) & 43 (in-part) remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed, at least in-part.

4. ***Priority***

Acknowledgment is made of Applicants' claim for priority based on applications filed in EPO on 12/02/1998 [98204018.0] & 03/12/1999 [99200739.3]. Certified copies of the documents have been received.

5. ***Claim Objections***

Claim 43 remain objected for reciting non-elected subject matter. Second half of the claim 43 still recites - 'or one or more isolated DNA sequences.....ester production in fruit', which subject matter has been previously restricted. In response to this Office Action Applicants are required to amend the claims deleting non-elected elected subject matter.

6. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

7. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

8. ***Claim Rejections - 35 USC §112*** (first paragraph)

Written description

Claim 43 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 43 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim is directed to a genus of polypeptide molecules with either SEQ ID NO: 6 or 31 or polypeptide having the limitations of a polypeptide having the amino acid sequence which is 55% identical to SEQ ID NO: 31 (claim 43).

Claim 43 is rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO: 31 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO: 31 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO: 31 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences derived from SEQ ID NO: 31, including variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of functions and with the potentiality of generating many different antibodies. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses two full length functional species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicants' Arguments:

Applicants argue that the amended claims recite both structure and function and thus meet the written description requirements.

Applicants are indeed correct as far as claims 19-21 & 34 are concerned. However, with respect to claim 43, the functional limitation with respect to modified SEQ ID NO: 6 (30%) [alcohol acyl dehydrogenase] and SEQ ID NO: 30 (55%) [alcohol dehydrogenase] is lacking.

9. ***Enablement***

Claims 19-21, 34 & 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an alcohol acyl transferase of SEQ ID NO: 6 and an alcohol dehydrogenase of SEQ ID NO: 31 (both from strawberry), does not reasonably provide enablement for any alcohol acyl transferase having 30%, 50% or 70% identity to SEQ ID NO: 6; or any alcohol dehydrogenase having 55% identity to SEQ ID NO: 31; or any fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of alcohol acyl transferases and alcohol dehydrogenases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequences of alcohol acyl transferase and alcohol dehydrogenase of SEQ ID NO: 6 & 31 respectively.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any alcohol acyl transferase with 30%, 50 or 70% identity to the enzyme of SEQ ID NO: 6, or all modifications of any alcohol dehydrogenase with 55% identity to the enzyme of SEQ ID NO: 31, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting alcohol acyl transferase or alcohol dehydrogenase activity; (B) the general tolerance of alcohol acyl transferase or alcohol dehydrogenase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any alcohol acyl transferase or alcohol dehydrogenase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including alcohol acyl transferase or alcohol dehydrogenase with an enormous number of amino acid modifications of the of SEQ ID Nos: 6 & 31. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of alcohol acyl transferase or alcohol dehydrogenase having the desired biological

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characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants' Arguments:

Applicants based upon the calculated % homology between some of the recently identified acyltransferases and SEQ ID NO: 6, argue that acyl transferases from banana, apple & melon have the same enzymatic activity and yet have less than 30% sequence homology with respect to strawberry [SEQ ID NO: 6], and are therefore enabled by the present specification.

Applicants' arguments are well taken, however, such diversity among the various fruit crops with respect to a single enzyme, further makes the job of one skilled in the art all the more difficult. Since a uniform strategy cannot be rationalized as to which amino acids or regions of the protein structure among the various species which may be modified and which may not be modified without effecting alcohol acyl transferase or alcohol dehydrogenase activities; and the extent of tolerance of the protein(s) to such modifications without effecting the desired enzymatic function remains highly unpredictable. The rejection is maintained for all of the above reasons and those already made of record.

10. Claim Rejections - 35 USC § 112 (second paragraph)

(a) Claims 34 & 43 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Amended Claim 34, line 7, recites the phrase 'C terminal end of the coding sequence if SEQ ID NO: 31'. The claims are indefinite because 'C terminal end is with reference amino acid sequence of SEQ ID NO: 31, and not 'coding sequence'. Deleting 'coding' and inserting 'amino acid' instead will overcome this part of the rejection.

Similar correction is required in claim 43, line 14.

(b) Claim 43 recite the phrase 'kit for screening ...volatile ester compounds'. The claim is indefinite because it is unclear how a kit comprising a polypeptide of SEQ ID NO: 6 or 31 or fragments thereof is sufficient in diagnosing 'volatile ester compound'. Suitable amendment and/or clarification is required to overcome this rejection.

11. **35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title".

New claims 46 is rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claim to recite wording such as "An isolated polypeptide".

12. Claim 45 is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

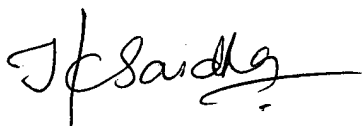
14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose

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telephone number is (571) 272-0940. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group in the Technology Center is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 571 272-1600.



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